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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LI, RUIXIANG	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
11/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,278	INBE ET AL.	
	Examiner	Art Unit	
	Ruixiang Li	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5 and 9-13* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 11-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 March 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group I, drawn to a method of screening for an agent that modulates P2Y15 activity, in the reply filed on 09/24/2007 is acknowledged. The traversal is on the ground(s) that methods of screening for agents that modulate P2Y15 activity might also identify agents that bind to P2Y15 polypeptide, since many agents that bind to P2Y15 polypeptide might modulate P2Y15 activity. Applicants' argument has been fully considered, but is not deemed to be persuasive because the inventions listed as Groups I and II are not so linked by the same or a corresponding special technical feature as to form a single general inventive concept as set forth in the restriction requirement. Thus, unity of invention is lacking and restriction is appropriate.

   The requirement is still deemed proper and is therefore made FINAL.

2. Applicants' preliminary amendments filed upon 03/25/2005 and 11/17/2005 are entered in full. Claims 6-8 and 14-18 are canceled. Claims 1-5 and 9-13 are pending. Claims 1-5 and 11-13 are under consideration. Claims 9 and 10 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 09/24/2007.

Drawings

3. The drawings filed on 03/25/2005 are accepted by the Examiner.

Claim Rejection —35 USC § 112, 1st paragraph

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5 and 11-13 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors that are considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claims 1-5 and 11-13 are drawn to a method for detecting the activity of P2Y15 in a sample or a method of screening for an agent to modulate P2Y15 activity

using cells expressing P2Y15, comprising detecting a signaling activity of P2Y15 polypeptide under conditions which allow binding of AMP or adenosine receptor ligand to P2Y15. The claims are broad because the term "P2Y15" encompasses a genus of P2Y15 homologues or variants (see page 15 of the specification). However, the specification merely discloses human, mouse and rat P2Y15 polypeptides set forth in SEQ ID NOS: 2, 4, and 6.

The specification and a post-filing date publication (Inbe et al. *J. Biol. Chem.* 279:19790-19799, 2004) in which the authors include the inventors teach that the human GPCR 80 of SEQ ID NO: 2 is a P2Y15 receptor for AMP and adenosine. However, the publications, either before the filing date or after the filing date of the instant application, teach that the human GPR80 (Lee et al., *Gene* 275:83-91, 2001) is not a genuine P2Y receptor. Abbracchio et al. (*Trends in Pharmacological Sciences* 26:8-9, 2005) teach the following reason why the human GPR 80 (also called GPR99) is not a P2Y15 receptor: (i), the phylogenetic distance of the protein sequence of this receptor from the known receptors for adenosine (bottom of left column to top of right column of page 8) and in the first original study of GPR99 (Wittenberger et al., *BMC Genomics* 3:17-22,2002), this receptor failed to respond to AMP in either the oocyte or the Chinese hamster ovary cell expression system; (ii). He and colleagues (He et al., *Nature* 429:188-193, 2004) reported that two orphan GPCRs, GRP99 and GPR 91 actually functioned as receptors for two citric acid cycle intermediates, α-ketoglutarate and succinate, respectively; (iii). HEK293 cells exclusively used in the study of Inbe et al. is known to express several endogenous

P2Y receptors in addition to the P1 adenosine receptor A_{2A} and A_{2B}, which might complicate the pharmacological characterization of novel receptors. Moreover, adenosine A1 and P2Y1 receptors have been shown previously to form heterodimers that enable the A1 receptor to bind and respond to ADP, and thus it is possible that , at least in part, response to AMP and adenosine in HEK293 cells expressing GPR80/GPR99 are influenced by a physical interaction between GPR80 /GPR99 and endogenous P2Y or A_{2B} receptors, resulting a novel pharmacological response profile (*Trends in Pharmacological Sciences* 26:8-9, 2005; left column of page 9); (iv) another study has shown that expression of GPR80/GPR99 in several cell lines (CHO, COS and another subclone of HEK293) did not result in responses to either adenosine or AMP (*Trends in Pharmacological Sciences* 26:8-9, 2005; left column of page 9). Abbracchio et al. conclude that the result of Inbe et al. were more likely to be due to high levels of expression of endogenous adenosine receptors in the clone of HEK293 cells expressing GPR80/GPR99, and/or to heterodimer formation or another artefact. Abbracchio et al. futher state that the P2Y receptor Nomenclature Subcommittee has decided that GPR/80/GPR99 is not a P2Y receptor for adenosine, AMP orther nucleotides, but instead is activated by citric acid cycle intermediates.

In view of the extensive teachings that contradict the instant disclosure, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

6. Claims 1-5 and 11-13 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter

which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-5 and 11-13 are drawn to a method for detecting the activity of P2Y15 in a sample or a method of screening for an agent to modulate P2Y15 activity using cells expressing P2Y15. Thus, the claims recite a genus of P2Y15 polypeptides (see page 15 of specification). However, the claims do not require that P2Y15 polypeptides possess any particular biological activity, nor any particular conserved structure, nor other disclosed distinguishing feature.

The instant disclosure of human, mouse and rat P2Y15 polypeptides set forth in SEQ ID NOS: 2, 4, and 6 does not adequately support the scope of the recited genus, which encompasses a substantial variety of P2Y15 homologues or variants (see page 15 of the specification). A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial

portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). While disclosing three P2Y15 polypeptides of SEQ ID NOSS: 2, 4, and 6, and their binding activity, the instant disclosure fails to provide sufficient description information, such as definitive structural or functional features of the recited genus of P2Y15 polypeptides. There is no description of the conserved regions that are critical to the function of the genus of P2Y15 polypeptides recited. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function.

Moreover, the prior art does not provide compensatory structural or correlative teachings to enable one skilled in the art to identify the encompassed P2Y15 polypeptides. In fact, the P2Y receptor Nomenclature Subcommittee has decided that GPR/80/GPR99 is not a P2Y receptor for adenosine, AMP orther nucleotides, but instead is activated by citric acid cycle intermediates (Abbracchio et al., *Trends in Pharmacological Sciences* 26:8-9, 2005).

Due to the breadth of the recited genus of P2Y15 polypeptides and lack of the definitive structural or functional features of the recited genus, one skilled in the art would not recognize from the disclosure that the applicant was in possession of the recited genus of P2Y15 polypeptides. Accordingly, only a method of employing a P2Y15 polypeptide set forth in SEQ ID NOS: 2, 4, and 6 meets the written description provision of 35 U.S.C. §112, first paragraph.

Claim Rejections—35 USC § 112, 2nd paragraph

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-5 and 11-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-5 and 11-13 are indefinite because they recite the acronym "P2Y15" Such a term is determined arbitrarily without a definitive structure. Others in the field may isolate the same protein and give an entirely different name. For example, the polypeptide is also named as "GPR80" or " GPR99" (Lee et al., *Gene* 275:83-91, 2001; Abbracchio et al., *Trends in Pharmacological Sciences* 26:8-9, 2005). Thus, reciting biochemical molecules by a particular name given to the protein by various workers in the field fails to distinctly pointing out what the protein is. Applicants should particularly point out and distinctly recite characteristics associated with the protein, such as a sequence identifier.

Claims 1 and 5 are indefinite because they recite "AMP or adenosine receptor ligand". Since neither the prior art nor the specification defines the term unambiguously, it is unclear what the metes and bounds of the term are, rendering claims indefinite.

Claims 1-5 and 11-13 are indefinite because the steps set forth in the methods do not necessarily achieve the goal set forth in the preamble because there is no assurance that a signaling activity measured is due to the activation of P2Y15 since

the AMP or adenosine receptor ligand may bind to other receptors present in a sample.

Conclusion

9. No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

Ruixiang Li

Ruixiang Li, Ph.D.
Primary Examiner
November 12, 2007

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